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Aggregation of amyloid Aβ(1-40) peptide in perdeuterated 2,2,2-trifluoroethanol caused by ultrasound sonication

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Abstract

Ultrasound sonication of protein and peptide solutions is routinely used in biochemical, biophysical, pharmaceutical and medical sciences to facilitate and accelerate dissolution of macromolecules in both aqueous and organic solvents. However, the impact of ultrasound waves on folding/unfolding of treated proteins, in particular, on aggregation kinetics of amyloidogenic peptides and proteins is not understood. In this work, effects of ultrasound sonication on the misfolding and aggregation behavior of the Alzheimer's Aβ (1-40)-peptide is studied by pulsed-field gradient (PFG) spin-echo diffusion NMR and UV circular dichroism (CD) spectroscopy. Upon simple dissolution of Aβ(1-40) in perdeuterated trifluoroethanol, CF3-CD--OD (TFE-d3), the peptide is present in the solution as a stable monomer adopting α-helical secondary structural motifs. The self-diffusion coefficient of Aβ(1 -40) monomers in TFE-d3 was measured as 1.35 × 10-10 m2 s-1, reflecting its monomeric character. However, upon ultrasonic sonication for less than 5 min, considerable populations of Aβ molecules (ca 40%) form large aggregates as reflected in diffusion coefficients smaller than 4.0 × 10-13 m2 s-1. Sonication for longer times (up to 40 min in total) effectively reduces the fraction of these aggregates in 1H PFG NMR spectra to ca 25%. Additionally, absorption below 230 nm increased significantly upon sonication treatment, an observation, which also clearly confirms the ongoing aggregation process of Aβ(1-40) in TFE-d3. Surprisingly, upon ultrasound sonication only small changes in the peptide secondary structure were detected by CD: the peptide molecules mainly adopt α-helical motifs in both monomers and aggregates formed upon sonication.

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Keywords

Alzheimer's Aβ(1-40) peptide, Deuterated trifluoroethanol, Peptide aggregation, Peptide secondary structure, Pulsed-field gradient 1H NMR, Translational self-diffusion